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AURELIO-04: A phase 2, open-label, single-arm, multicenter study to determine the efficacy and safety of SOT101 in combination with pembrolizumab in patients with selected advanced solid tumors

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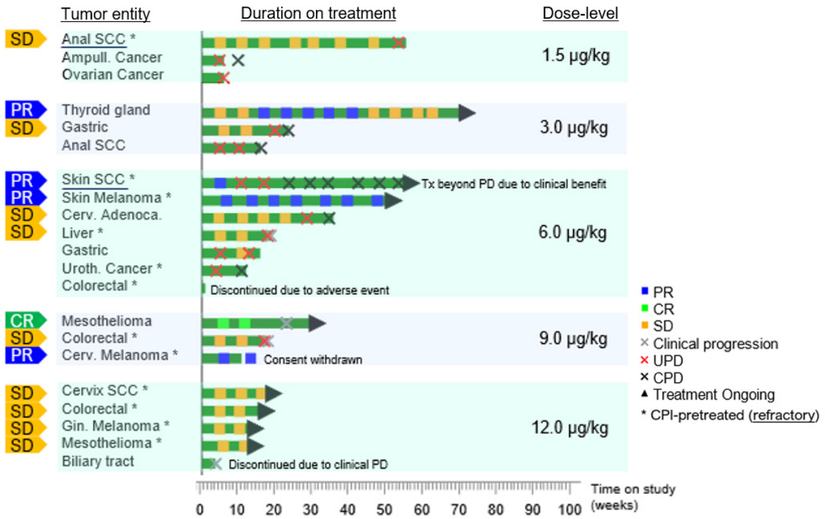
Background

- SOT101 (INN: nanrilkefusp alfa) is a fusion protein of IL-15 and the IL-15 receptor α sushi+ domain.
- SOT101 was investigated in the phase 1 dose-escalation study AURELIO-03 (NCT04234113) as monotherapy and in combination with pembrolizumab.
- In the combination part of AURELIO-03, 21 patients were treated at SOT101 dose levels of 1.5 to 12.0 µg/kg on days 1, 2, 8, 9 plus pembrolizumab 200 mg on day 1 every 3 weeks.
- Maximum activation of NK cells was observed already at low dose levels, maximum $CD8^+$ T-cell activation was reached at doses from 9 to 12 µg/kg SOT101 with no relevant effect on Treg cells.
- 12 µg/kg SOT101 was selected as the combination RP2D, same as for SOT101 monotherapy.
- SOT101 in combination with pembrolizumab was well tolerated. AEs were mainly grade 1/2 and transient. There was no additive toxicity when combining SOT101 with pembrolizumab.
- SOT101 in combination with pembrolizumab resulted in clinical benefit in most patients, even in CPI-refractory tumors [1,2].

AURELIO-03 phase 1 interim efficacy of SOT101 in combination with pembrolizumab



Clinical benefit* was reported in 15 out of 19 patients with at least one post-baseline tumor assessment:

- 1 confirmed CR
- 4 PRs; 3 PRs confirmed
- 10 SD; 9 SD ≥2 or more assessments

* Considered as at least one occurrence of SD or response

Data presented at ASCO 2022 [2]

Study design

- AURELIO-04 (NCT05256381) is a phase 2, open-label, single-arm, multicenter study of SOT101 in combination with pembrolizumab to evaluate the efficacy and safety in patients with the following selected advanced solid tumor indications:

- **Non-small cell lung cancer**
  - 2nd or 3rd line with disease progression on or after a CPI- and/or platinum-containing regimen, with no EGFR or ALK genomic tumor aberrations
- **Colorectal cancer**
  - 1st line with unresectable or metastatic MSI-H/dMMR colorectal cancer
- **Cutaneous SCC**
  - 1st line with recurrent or metastatic cutaneous SCC or 2nd line if refractory or relapsed after a CPI-containing regimen
- **Hepatocellular carcinoma**
  - 2nd or later line after progression on or after a CPI-containing regimen
- **mCRPC**
  - 2nd or later line after recurrence or failure of docetaxel
- **Ovarian cancer**
  - 2nd or later line after recurrence or failure on platinum-based therapy within 6 months

- Solid tumor selection is based on previous pembrolizumab studies and/or data with other CPIs and includes both CPI-relapsed and/or CPI-naïve tumors.
- A total of up to approximately 320 patients will be included, maximum 50 to 57 per indication.

- **Key eligibility criteria**
  - Measurable disease as per RECIST 1.1 (mCRPC: a defined number of patients with non-measurable disease allowed)
  - Accessible tumor tissue for biopsy
  - ECOG PS 0-1
  - Adequate organ function
  - No prior IL-2 or IL-15 therapy

Study treatment
SOT101 12 µg/kg s.c. on days 1, 2, 8, 9 in combination with pembrolizumab i.v. 200 mg on day 1 every 3 weeks

Disease progression or unacceptable toxicity

- **Primary objective**
  - To estimate the anti-tumor efficacy of SOT101 in combination with pembrolizumab according to RECIST 1.1 by means of ORR, for each indication or disease cohort separately
- **Status**
  - The study will enroll patients in Europe and in the United States.
  - FPI was in June 2022.

Primary endpoint

- ORR according to RECIST 1.1 in patients with measurable disease

Secondary endpoints

- Type, frequency, and severity of TEAEs; AEs of special interest; safety laboratory findings; vital signs; ECG findings
- Additional efficacy endpoints:
  - iORR in patients with measurable disease according to iRECIST
  - (i)BOR, (i)TtR in patients with measurable disease according to RECIST 1.1 and iRECIST
  - (i)DoR, (i)CBR, (i)PFS according to RECIST 1.1 and iRECIST and for mCRPC per PCWG3-modified RECIST 1.1
  - mCRPC only: CTC count conversion, confirmed PSA decline of ≥50%, time to confirmed PSA progression
- Plasma concentrations of SOT101 over time
- Incidence, titer, and time course of anti-drug antibodies against SOT101

Exploratory endpoints

- Changes in the expression of immune biomarkers as compared to baseline in tumor tissue; circulating tumor DNA fraction (mCRPC only); status of immune, molecular, disease-related, and other exploratory biomarkers in blood and archival and/or freshly obtained tumor tissue
- Overall survival

Statistics

- No formal testing of statistical hypotheses is planned, analyses will be descriptive. Considering benchmark ORRs, a futility analysis is planned for each indication separately. Exploratory analyses include immune and molecular biomarkers.

References

1. Champiat S, et al: SOT101, an IL-2/IL-15 Rβγ superagonist, in combination with pembrolizumab in patients with advanced solid tumors: Interim safety and efficacy results from the AURELIO-03 dose escalation trial. Presented at: American Association for Cancer Research Annual Meeting 2022; April 8-13, 2022; New Orleans, LA.
2. Garralda E, et al. , et al. Interim safety and efficacy results from AURELIO-03, a phase 1 dose escalation study of the IL-2/IL-15R βγ receptor superagonist SOT101 as a single agent and in combination with pembrolizumab in patients with advanced solid tumors. Presented at: American Society of Clinical Oncology Annual Meeting 2022; June 3-7, 2022; Chicago, IL.

Abbreviations: AE, adverse event; ALK, anaplastic lymphoma kinase; BOR, best overall response; CBR, clinical benefit rate; CPD, confirmed progressive disease; CPI, immune checkpoint inhibitor; CTC, circulating tumor cell; CR, complete response; DoR, duration of response; ECG, electrocardiography; ECOG PS, Eastern Cooperative Oncology Group performance status; eCRF, electronic case report form; EGFR, epidermal growth factor receptor; FPI, first patient in; IL, interleukin; INN, international nonproprietary name; iRECIST, Response Evaluation Criteria In Solid Tumors for immune-based therapeutics; i.v., intravenously; mCRPC, metastatic castration-resistant prostate cancer; MSI-H/dMMR, microsatellite instability-high/mismatch repair deficient; NK, natural killer; ORR, objective response rate; PCWG, Prostate Cancer Clinical Trials Working Group; PD, progressive disease; PFS, progression-free survival; PR, partial response; PSA, prostate-specific antigen; RECIST, Response Evaluation Criteria In Solid Tumors; RP2D, recommended phase 2 dose; s.c., subcutaneously; SCC, squamous cell carcinoma; SD, stable disease; TEAE, treatment-emergent adverse event; Treg, regulatory T cell; TtR, time to response; UPD, unconfirmed progressive disease

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This study is in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.